Exhibit B

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Original Article

Transobturator vs Single-Incision Suburethral Mini-slings for Treatment of Female Stress Urinary Incontinence: Early Postoperative Pain and 3-Year Follow-up

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ABSTRACT **Study Objective:** To compare related pain and cure using the transobturator and single-incision suburethral mini-sling anti-incontinence operations.

Design: Open, prospective, nonrandomized 2-armed study comparing 2 surgical procedures for treatment of female stress urinary incontinence (Canadian Task Force classification II-1).

Setting: A university and a private hospital.

Patients: One hundred sixty-two women with stress urinary incontinence underwent either a tension-free vaginal tape–obturator (TVT-O) or a single-incision (TVT-SECUR) suburethral or mid-urethral tape operation.

Measurements and Main Results: Pain levels were estimated using a visual analog scale, and outcome using the Urinary Distress Inventory and the Incontinence Impact Questionnaire. Postoperative vaginal and thigh pain was transient, lasting for up to 2 weeks, and occurred significantly more frequently in the TVT-O group (32% vs 1% and 32% vs 0%, respectively). Dyspareunia was not self-limited, and occurred more frequently in the TVT-SECUR group (7.9% vs 0%). Cure rates were 86.9% in the TVT-O group and 90.9% in the TVT-SECUR group. Complication rates were similar in the 2 groups.

Conclusion: Both procedures were effective, with few adverse effects. In sexually inactive patients, the TVT-SECUR procedure may be preferable because thigh and vaginal pain is largely averted with this procedure. Sexually active patients might be better referred for the TVT-O procedure because it was not followed by dyspareunia in our series. Patient choice of surgical method rather than randomization weakened the strength of this study. Journal of Minimally Invasive Gynecology (2011) 18, 769–773 © 2011 AAGL. All rights reserved.

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Tension-free vaginal tape–obturator (TVT-O) is a surgical procedure for treatment of female stress urinary incontinence (SUI). The operation, described by de Leval in 2003 [1], is based on transobturator placement of a polypropylene tension-free mid-urethral supportive sling, and is now accepted worldwide. The TVT-O procedure was designed to overcome some operative complications associated with the retropubic tension-free vaginal tape procedure [2–4]. Complications were rare and included bladder penetration, postoperative urinary outlet obstruction, bowel penetration, and intraoperative and postoperative bleeding [5–8]. These adverse effects were attributed to retropubic needle passage, proximal to the bladder, bowel, and blood vessels. The TVT-O procedure, designed to avoid the retropubic space, was observed to yield high success rates and low complication rates, and, therefore, became popular. Nevertheless, after TVT-O surgery, some women developed postoperative thigh pain [9,10].

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The TVT-SECUR system (Gynecare, division of Ethicon, Inc., Somerville, NJ) is a mini suburethral mid-urethral single-incision sling that does not pass through the obturator membrane. It is introduced with metallic inserters only to the level of the internal obturator muscles, through the relatively safe medial side of the anterior pelvic floor compartment, avoiding the pelvic viscera and vessels. The TVT-SECUR procedure is regarded by many [11–14], although not by all [15], as effective, with little postoperative pain.

The objective of the present study was to analyze and compare the midterm outcomes of these 2 minimally invasive anti-incontinence procedures.

Patients and Methods

The study was an open, prospective, nonrandomized, 2-armed study that compared 2 surgical procedures for treatment of female SUI: the TVT-O and the TVT-SECUR. The study patients had not been included in previous publications.

Given that the previously reported cure and complication rates associated with these 2 surgical procedures were similar, sample size calculation was based on reports that demonstrated an incidence of significant postoperative pain of 25% with the TVT-O [9,10] and 5% with the TVT-SECUR [11–14].

The study was approved by our institutional review board (Helsinki Committee). The inclusion criterion was a diagnosis of SUI based on the patient's personal history and a positive cough test with the bladder holding 300 to 400 mL. Exclusion criteria included patient refusal to participate, presence of a connective tissue disorder, or the need for concomitant surgery other than colporrhaphy. The study patients were provided with detailed relevant information, both written and verbal, about both procedures before they signed the consent form. They were then asked to choose either the TVT-O or the TVT-SECUR procedure as the anti-incontinence operation, with respect for their right to make an informed decision about the operative method.

All operations were performed by a single surgeon (M.N.). At 1 hour before surgery, all patients were given 1 g cefonicid (Monocef; SmithKline Beecham, PLC, Brentford, Middlesex, England) intravenously. They all underwent an iodine antiseptic vaginal wash before surgery. The mode of anesthesia was per patient request. Urinary bladder catheterization or diagnostic cystoscopy were not routinely performed. Patients with vaginal wall relaxation underwent anterior and/or posterior colporrhaphy, concomitant with the anti-incontinence surgery. The TVT surgical needle was inserted using the technique described by de-Leval [1] for TVT-O and by Neuman [11] for TVT-SECUR, with the hammock method. Patients were followed up at 1, 6, and 12 months after surgery and yearly thereafter.

Data were collected from patient medical records by researchers not involved with patient care. Subjective data about urgency, frequency, stress and urge incontinence of urine and feces, impairment of sexual function, voiding habits, and pelvic pain and bulging were recorded prospectively at the first postoperative visit using a visual analog scale for pain, and validated Urinary Distress Inventory–6 and the Incontinence Impact Questionnaire–7 at every follow-up visit. Dyspareunia and level 3 or higher vaginal and thigh pain on the visual analog scale were regarded as significant. Objective outcome was assessed via pelvic examination and cough test with a filled bladder. The terminology used for prolapse and incontinence was that of the International Continence Society/International Urogynecological Association standardization committee. The primary outcome measures for the study were the frequency, patterns and levels of postoperative pain and dyspareunia, data collected at the end of the first postoperative course. Secondary outcome measures were the overall cure rates and surgery-related adverse effects with the 2 operations with 36 months of follow-up.

Operative outcome was graded as follows: "cure" when there was no leakage at all, "improvement" when the leakage was significantly reduced and patients did not request further treatment, and "failure" when there was indication for repeat operation. Normally distributed continuous data were described using the mean and standard deviation, and the median and interquartile range for data not fitting a normal distribution. Categorical data were described using numbers and percentages.

All statistical analyses were performed using commercially available software (SPSS version18; SPSS, Inc., Chicago, IL). The *t* test was used for comparison of quantitative variables between groups, and the χ^2 test or Fisher exact test were used to compare categorical variables between groups. The McNemar test was used to compare longitudinal data. For all statistical tests, $p = .05$ (1-tailed) was considered significant. One hundred sixty patients each were required in the TVT-O and TVT-SECUR arms to detect a 20% increase in the postoperative pain rate, with 80% power and 95% confidence (.05 significance).

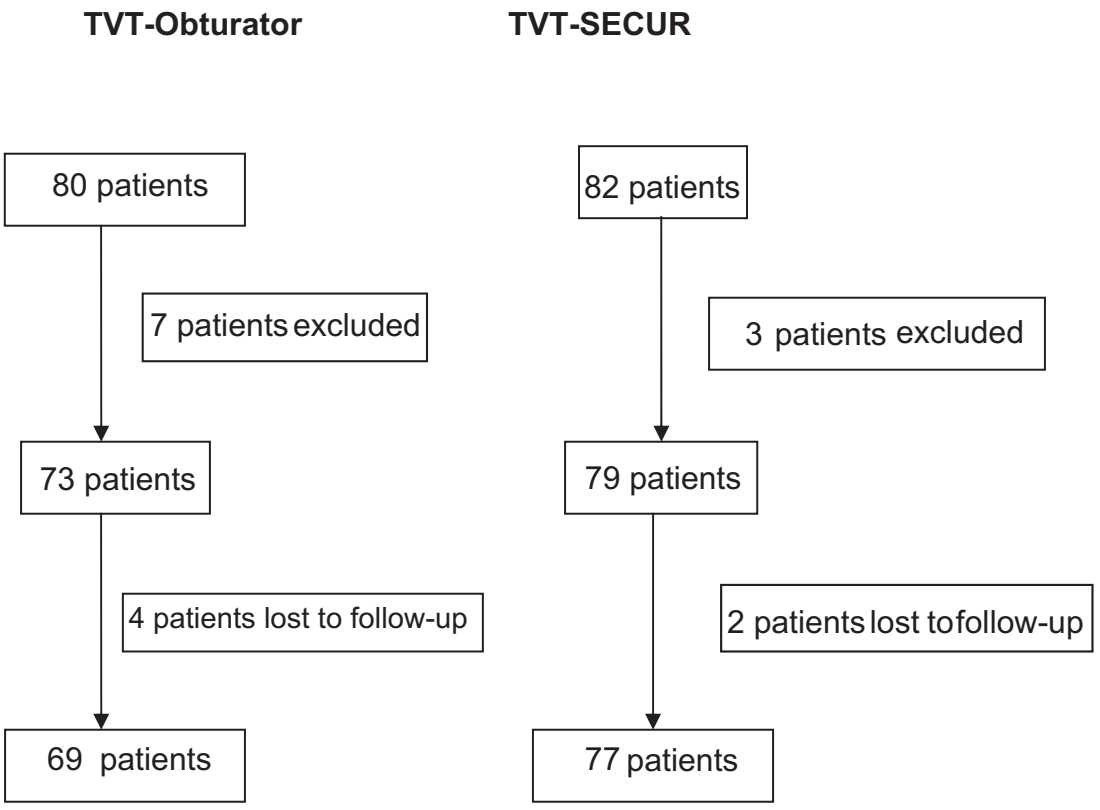
Results

One hundred sixty-two patients with SUI were referred for corrective surgery. Patients were recruited over 17 months. Seven patients who underwent the TVT-O procedure (8.8%) and 3 patients who underwent the TVT-SECUR procedure (3.8%) were excluded from the study because of refusal to participate, the need for concomitant operations other than anterior or posterior colporrhaphy, or presence of connective tissue disorders (Fig. 1). The study patients either failed or refused pelvic floor rehabilitation physical therapy.

Insofar as patient personal characteristics preoperatively, no statistical differences were observed between the 2 groups except for a higher occurrence of urinary urgency in the TVT-SECUR group (Table 1). Age, parity, menopause, bladder overactivity, previous anti-incontinence surgery, and the presence of chronic illnesses were similar between the 2

Fig. 1

Patient flow chart.



patient groups (Table 1). There was no difference between the groups insofar as operative details including the duration of the procedure and the need for concomitant colporrhaphy (Table 2). Operative injuries and cure rates, as well as postoperative complication rates were similar in the 2 groups. The only outcome measures with statistically significant difference between the groups were postoperative pain levels and frequency of dyspareunia (Tables 3 and 4). Significant vaginal and thigh pain, with VAS score higher than 3, occurred more frequently with TVT-O (32% vs 1%) than with the TVT-SECUR procedure (32% vs 0%), respectively. Thigh pain was transient and lasted no longer than 2 weeks. De novo dyspareunia occurred only in women who underwent the TVT-SECUR (5 of 77 patients; 7.9% vs 0%) and was not self-limited. Patients with tape-related dyspareunia underwent segmental tape removal, either in the office or the operating room, to relieve pain.

Four patients in the TVT-O group (5.4%) and 2 in the TVT-SECUR group (2.6%) were lost to follow-up (Table 1). However, data for these patients who dropped out did not alter the study results or conclusions [16].

A single event of operative bleeding in the TVT-SECUR group was managed using a surgical hemostatic suture via the vaginal approach [17]. No patients required blood transfusion. One event of tape exposure in the TVT-O group was treated successfully in the office by simply removing the extruded mesh segment. Cure rate was 86.9% for the TVT-O group and 90.9% for the TVT-SECUR group. Patients who experienced therapeutic failure were evaluated using urodynamic tests, ultrasound, and cystoscopy, and

Table 1

Patient characteristics[a]

Variable	TVT-Obturator group (n = 73)	TVT-SECUR group (n = 79)	p Value
Age, yr	54 (11.8)	53 (10.6)	.55
Parity	2.8 (1.0)	2.7 (1.0)	.52
USI duration, yr	3.8 (4.8)	4.3 (5.6)	.58
Postmenopausal	49 (67.1)	44 (55.7)	.43
Urgency	28 (37.8)	42 (54.5)	.02
Frequency	24 (32.4)	33 (42.9)	.12
Nocturia	19 (25.7)	14 (24.7)	.27
Cystocele	51 (68.9)	63 (81.8)	.68
Rectocele	35 (47.3)	50 (64.9)	.73
Previous USI corrective surgery	3 (4.2)	3 (3.9)	.135
Underlying chronic illness	9 (12.5)	11 (14.3)	.21

USI = urinary stress incontinence.
[a] Values are given as mean (SD) or No. of patients (%).

Table 2

Operative details[a]

Variable	TVT-Obturator group (n = 73)	TVT-SECUR group (n = 79)	p Value
Sling operative time, min	17 (12–27)	14 (10–19)	.28
Concomitant colporrhaphy			
Anterior colporrhaphy	51 (68.9)	63 (81.8)	.52
Posterior	35 (47.3)	50 (64.9)	.47

[a] Values are given as mean (range) or No. of patients (%).

then were offered tape tightening via a TVT readjustment procedure [18]. Early postoperative partial urinary outlet obstruction, leading to increased residual bladder volume (>150 mL) occurred in 9 patients, 6 in the TVT-O group (8.2%) and 3 in the TVT-SECUR group (3.9%). This was treated using intermittent bladder catheterization for up to 1 week. Complete obstruction occurred in 4 patients, 2 in each group, and was treated in the operating room via release of the tape tension [19].

Discussion

The primary findings of the present study including incidence, patterns, and levels of postoperative pain and dyspareunia differed significantly between the 2 patient groups. The incidence of postoperative pain in the TVT-O group was statistically significantly higher than in the TVT-SECUR group. The pain was located in the vagina and the thigh, lasted for up to 2 weeks, responded well to oral analgesic therapy, and resolved spontaneously. There is no clear explanation for the pain in the TVT-O group and its subsequent resolution because there is usually no overt nerve injury associated with this procedure. It might possibly be due to tissue damage in the obturator region, with subsequent spontaneous healing and recovery. These findings

Table 3

Intraoperative and early postoperative complication rates[a]

Variable	TVT-Obturator group (n = 73)	TVT-SECUR group (n = 79)	p Value
Bladder, bowel, or urethral injury	0	0	NA
Operative blood loss >100 mL	0	1 (0.0)	4.80
Vaginal mesh protrusion	1 (1.4)	0	1.00
Operative field infection	0	0	NA
Early voiding difficulty	4 (5.4)	9 (11.7)	.15
Postoperative UTI	1 (1.4)	1 (1.3)	.99

NA = not available; UTI = urinary tract infection.
[a] Values are given as No. of patients (%).

Table 4

Operative outcome[a]

Variable	TVT-Obturator group (n = 60)	TVT-SECUR group (n = 77)	p Value
Early postoperative vaginal pain	22 (31.8)	1 (1.3)	<.001
Early postoperative thigh pain	22 (31.8)	0	<.001
USI cure	60 (86.9)	70 (90.9)	.18
USI marked improvement	2 (2.7)	4 (5.2)	.19
Operative failure	7 (10.1)	3 (3.9)	.12
Postoperative nocturia	14 (18.9)	4 (5.2)	.11
Postoperative frequency	9 (12.2)	12 (15.6)	.69
Postoperative urgency	14 (18.9)	12 (15.6)	.10
Postoperative dyspareunia	0	5 (7.9)	.03

USI = urinary stress incontinence.
[a] Values are given as No. of patients (%).

are in accordance with previous publications that reported postoperative thigh pain in as many as 25% of patients who underwent the TVT-O procedure. The pain usually lasted for up to a week and was rarely permanent [9,10]. TVT-SECUR is associated with less pain [11], probably because it does not traverse the obturator membrane.

Dyspareunia occurred only in patients who underwent the TVT-SECUR procedure. The pain was relieved after surgical removal of the involved tape segment. Dyspareunia associated with the TVT-SECUR procedure might be explained in part by the rigidity and reduced flexibility of the synthetic polypropylene implant because it is laser cut, which tends to result in a stiff tape edge. As a result, the overlying vaginal mucosa is constantly traumatized, much more than it would be with use of mechanically cut tape. Both the TVT-O and TVT-SECUR techniques achieved similar urinary incontinence cure rates, with similar rates of adverse effects. The study was open and prospective, with 2 patient groups and 36 months of follow-up. The 2 patient groups studied were comparable insofar as demographic and personal data. The only dissimilarity was related to the incidence of urinary urgency, which was higher in the TVT-SECUR group; however, that discordance did not affect the study outcome because the cure rates were similar. Common complications of former retropubic operations for treatment of SUI such as pelvic and abdominal organ injury and bladder penetration are rare with use of the TVT-O and TVT-SECUR [8,11] because the tape introducers do not cross the retropubic area.

Operative time, need for concomitant colporrhaphy, and early and late postoperative complications were similar in the 2 study groups. The 3-year follow-up data presented herein agree in general with the previously reported efficacy of both the TVT-O and the TVT-SECUR in terms of cure and intraoperative and postoperative complication rates.

Although diagnostic cystoscopy was not performed in the study patients, we assumed that no bladder perforation occurred in these patients because no signs suggestive of bladder perforation (e.g., urinary leakage through surgical vaginal cuts) were recorded. Neither the TVT-O nor the TVT-SECUR was associated with postoperative field infection. Significant intraoperative bleeding occurred in only 1 patient, and voiding difficulties occurred at previously reported rates.

The data reported herein demonstrate that both the TVT-O and the TVT-SECUR procedures are associated with satisfactory cure rates and low complication rates. Sexually inactive patients might benefit from TVT-SECUR because of the low incidence of postoperative vaginal and thigh pain, whereas those who are sexually active might prefer the TVT-O procedure because of the low incidence of postoperative dyspareunia. Because the number of patients who received hormone therapy was small in these study groups, conclusions cannot be drawn about any potential hormonal influence on the outcome. The study design is underpowered and inherently limited because it is a nonrandomized two arm cohort study. In addition, there may have been potential selection bias because patients were grouped into the different arms by self-selection rather than randomization.

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